

NEUROPEPTIDE Y RECEPTOR SUBTYPES IN MAMMALIAN BRAIN: EVIDENCE FOR A BIBP3226 INSENSITIVE BINDING SITE LABELED WITH [125 I][LEU 31 ,PRO 34]PYY, Y. Dumont and R. Quirion, Douglas Hospital Research Center and Dept. Psychiatry, McGill University, 6875 Boul. LaSalle, Verdun, Quebec, Canada, H4H 1R3.

Neuropeptide Y (NPY) is one of the most abundant peptides present in the mammalian brain. This peptide has been implicated in several CNS functions including feeding and anxiety-related behaviors. Thus far, at least four receptor subtypes have been characterized and designated as Y $_1$, Y $_2$, Y $_3$ and Y $_4$ /PP $_1$ (The Physiologist, 38: A241-A261, 1995). Additionally, NPY binding sites have been detected in several species (Martel et al., Brain Res., 419: 403-407, 1987) and autoradiographic studies have shown that the Y $_1$ and Y $_2$ subtypes are most abundant in the rat brain cortex and hippocampus, respectively (Dumont et al., J. Neurosci., 13: 73-86, 1993). Recently, comparative autoradiographic studies have revealed some difference in the distributional profile of the radiolabelled Y $_1$ agonist, [125 I][Leu 31 ,Pro 34]PYY and antagonist, [3 H]BIBP3226 (Dumont et al., NeuroReport, In Press). In fact, membrane homogenates and autoradiographic binding studies revealed that the rat brain contains two populations of [125 I][Leu 31 ,Pro 34]PYY/Y $_1$ -like sites, one that is highly sensitive to the Y $_1$ antagonist, BIBP3226 while the other is not. The pharmacological profile of various analogues and fragments of NPY, PYY and PP to compete for [125 I][Leu 31 ,Pro 34]PYY/BIBP3226-insensitive sites is similar but not identical to the newly cloned Y $_4$ /PP $_1$ receptor subtype (hPP \geq PYY \geq NPY \geq [Leu 31 ,Pro 34]PYY \gg rPP = NPY $_{13-36}$ = PYY $_{13-36}$ = aPP). Finally, we recently noted major species differences in the CNS distribution of [125 I][Leu 31 ,Pro 34]PYY/Y $_1$ -like, [125 I]PYY- $_{36}$ /Y $_2$ -like and [125 I][Leu 31 ,Pro 34]PYY/BIBP3226-insensitive binding sites. While the rat and mouse brains demonstrated rather similar distribution profile, guinea pig and primate brains expressed very low levels of the Y $_2$ and Y $_1$ subtype, respectively. Accordingly, care must be taken when extrapolating from one species to another on the characteristics of brain NPY receptor subtypes. This study was supported by the MRC of Canada.